94061918 MEDLINE
DN 94061918
TI Proteolysis at the secretase and amyloidogenic cleavage sites of the **beta-amyloid** precursor protein by **acetylcholinesterase** and butyrylcholinesterase using model peptide substrates.
AU de Serres M; Sherman D; Chestnut W; Merrill B M; Viveros O H; Diliberto E J Jr
CS Division of Pharmacology, Burroughs Wellcome Co., Research Triangle Park, North Carolina 27709.
SO CELLULAR AND MOLECULAR NEUROBIOLOGY, (1993 Jun) 13 (3) 279-87. Journal code: CPX. ISSN: 0272-4340.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199403
AB 1. It was recently proposed that **acetylcholinesterase** (AChE), in addition to its esteratic activity, has proteolytic activity such that it may cleave the **beta-amyloid** precursor (beta-APP) within the beta-amyloid sequence. The purpose of this paper was to examine further whether AChE or butyrylcholinesterase (BuChE) had associated proteinase activity that was involved in the metabolism of beta-APP. 2. The ability of various preparations of AChE and BuChE to hydrolyze two synthetic fragments of beta-APP695 as model substrates containing the normal and aberrant cleavage sites was studied. 3. Digestion of these synthetic substrates with commercial preparations of Electrophorus electricus AChE indicated the presence of a trypsin-like proteolytic activity cleaving each peptide at the carboxy-terminal side of an internal lysine residue. 4. Purification of the trypsin-like proteinase activity by aminobenzamidine affinity chromatography yielded a preparation that was devoid of AChE activity but retained all of the proteinase activity. 5. Amino-terminal sequence analysis of this preparation showed that the first 13 amino acid residues were identical to beta-pancreatic trypsin. 6. These data indicate that the proteinase activity found in these commercial preparations of AChE is due to contamination with trypsin.
TI Proteolysis at the secretase and amyloidogenic cleavage sites of the **beta-amyloid** precursor protein by **acetylcholinesterase** and butyrylcholinesterase using model peptide substrates.
AB 1. It was recently proposed that **acetylcholinesterase** (AChE), in addition to its esteratic activity, has proteolytic activity such that it may cleave the **beta-amyloid** precursor (beta-APP) within the beta-amyloid sequence. The purpose of this paper was to examine further whether AChE or butyrylcholinesterase (BuChE). . .

TI Colocalization of cholinesterases with beta amyloid protein in aged and Alzheimer's brains.

AU Moran M A; Mufson E J; Gomez-Ramos P

CS Morphology Department, School of Medicine, Autonomous University of Madrid, Spain.

NC AG09466 (NIA)
AG10161 (NIA)

SO ACTA NEUROPATHOLOGICA, (1993) 85 (4) 362-9.
Journal code: 1CE. ISSN: 0001-6322.

CY GERMANY: Germany, Federal Republic of

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199307

AB The colocalization of beta amyloid protein with the enzymes acetyl- and butyrylcholinesterase was assessed using immunocytochemistry for beta amyloid protein and a sensitive histochemical technique for cholinesterases. In non-demented aged and Alzheimer's disease brains, double-stained sections for cholinesterases and thioflavin-S showed that all thioflavin-S-positive plaques were also positive for cholinesterases, indicating the presence of these enzymes in all plaques with beta-pleated amyloid protein. When amyloid angiopathy was present, cholinesterases were also observed in amyloid-laden vessels walls. Comparison of series of adjacent sections alternatively stained for **acetylcholinesterase**, **beta amyloid** protein and butyrylcholinesterase, as well as by double histo-immunocytochemical staining, showed either cholinesterase in a proportion of the preamyloid diffuse plaques. These data indicate that cholinesterases are associated with the amyloid protein from very early stages, when the beta-pleated structure is being formed. Novel functions attributed to acetyl- and butyrylcholinesterase, such us their proteolytic activity either by themselves or in association with heparan sulfate proteoglycans, may play a role in the aggregation or the consolidation processes taking place at the early stages of diffuse plaque formation.

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TI The acute neurotoxicity and effects upon cholinergic axons of intracerebrally injected beta-amyloid in the rat brain.

AU Emre M; Geula C; Ransil B J; Mesulam M M
CS Bullard and Denny-Brown Laboratories, Beth Israel Hospital, Boston, MA 02215.

NC AG05134 (NIA)
NS20285 (NINDS)
AG10282 (NIA)
SO NEUROBIOLOGY OF AGING, (1992 Sep-Oct) 13 (5) 553-9.
Journal code: NX5. ISSN: 0197-4580.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199303

AB The acute neurotoxicity and effects upon cholinergic axons of an intracerebrally injected synthetic peptide corresponding to the first 1-40 amino acids of beta-amyloid protein (beta AP1-40) was studied in rats. A synthetic peptide with the reverse sequence (beta AP40-1) or the vehicle alone were injected in the contralateral hemisphere as control. The size of the resulting lesions was quantified in serial sections using an image analyzer. Counts of cholinergic and noradrenergic fibers were also obtained around the lesion area. The results revealed that beta AP1-40 was significantly more toxic than both reverse peptide and the vehicle. The latter two, however, also caused considerable neurotoxicity. beta AP1-40 was toxic to both cholinergic and noradrenergic fibers to the same extent, and this toxicity was limited to the immediate vicinity of the lesion. This study confirms and extends the results of previous studies reporting neurotoxic effects of intracerebrally injected **beta-amyloid** in the rat. Our results also show that beta AP1-40 itself is not the source of the altered **acetylcholinesterase** enzyme activity that has been described in the plaques and tangles of Alzheimer's disease.

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L5 ANSWER 5 OF 9 MEDLINE
AN 1998180843 MEDLINE
DN 98180843
TI Beta-amyloid(Phe(SO3H)24)25-35 in rat nucleus basalis induces behavioral dysfunctions, impairs learning and memory and disrupts cortical cholinergic innervation.
AU Harkany T; O'Mahony S; Kelly J P; Soos K; Toro I; Penke B; Luiten P G; Nyakas C; Gulya K; Leonard B E
CS Central Research Division, Haynal Imre University of Health Sciences, Budapest, Hungary.
SO BEHAVIOURAL BRAIN RESEARCH, (1998 Feb) 90 (2) 133-45.
Journal code: AG3. ISSN: 0166-4328.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199807
EW 19980705
AB Long-term behavioral effects, changes in learning and memory functions and

aberrations of cholinergic fibers projecting to the parietal cortex were investigated after bilateral injections of beta-amyloid(Phe(SO3H)24)25-35 peptide in rat nucleus basalis magnocellularis (nbm). The beta-amyloid peptide used in these experiments contained the original beta-amyloid 25-35 sequence which was coupled to a phenylalanine-sulphonate group at position 24. This additional residue serves as a protective cap on the molecule without influencing its neurotoxic properties and results in water-solubility, stability and low rates of peptide metabolism. In this paper, home cage, locomotor and open-field activities, passive shock-avoidance and 'Morris' water maze learning abilities were assessed throughout a 35-day survival period. Subsequently, **acetylcholinesterase** (AChE) histochemistry was used to visualize alterations of parietal cortical cholinergic innervation. In response to the neurotoxic action of **beta-amyloid** (Phe(SO3H)24)25-35, a progressive hyperactivity developed in the rats in their home cages which were maintained throughout the 5-week post-injection period. This was accompanied by a significant hypoactivity in the novel environment of a locomotor arena. Beta-amyloid(Phe(SO3H)24)25-35-treated animals showed greatly impaired cortical memory functions in the step-through passive shock-avoidance paradigm, while spatial learning processes remained unaffected. Moreover, beta-amyloid(Phe(SO3H)24)25-35 injections in the nucleus basalis suppressed explorative behavior in rats and inhibited conditioned stress responses 28 days after surgery. Reductions of cortical cholinergic (AChE-positive) projections provided anatomical substrate for the behavioral changes. This indicated extensive, long-lasting neurodegenerative processes as a result of beta-amyloid(Phe(SO3H)24)25-35 infusion.
AB . . . locomotor and open-field activities, passive shock-avoidance and 'Morris' water maze learning abilities were assessed throughout a 35-day survival period. Subsequently, **acetylcholinesterase** (AChE) histochemistry was used to visualize alterations of parietal cortical cholinergic innervation. In response to the neurotoxic action of **beta-amyloid**(Phe(SO3H)24)25-35, a progressive hyperactivity developed in the rats in their home cages which were maintained throughout the 5-week post-injection period. This. . .

TI The adhesion function on acetylcholinesterase is located at the peripheral anionic site.

AU Johnson G; Moore S W
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SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1999 May 19) 258 (3) 758-62.
Journal code: 9Y8. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199908
EW 19990804

AB There is accumulating evidence that **acetylcholinesterase** has secondary noncholinergic functions, related to adhesion, differentiation, and the deposition of **beta-amyloid** in Alzheimer's disease. We have observed that the specific **acetylcholinesterase** peripheral anionic site inhibitors, BW284c51 and propidium iodide, abrogated cell-substrate adhesion in three human neuroblastoma cell lines. The active-site inhibitors, eserine and edrophonium, in contrast, had no effect. Certain anti-AChE antibodies were also shown to inhibit adhesion. Of these, the most effective were a monoclonal (E8) and a polyclonal having cholinesterase-like catalytic activity. These were raised against an acetylcholinesterase-inhibitor complex, implying that the epitope is associated with active-site structures. Two other monoclonal antibodies (E62A1 and E65E8) partially inhibited adhesion. The epitopes of these antibodies have been shown to overlap the peripheral anionic site of acetylcholinesterase. Competition ELISA between the monoclonal antibodies and inhibitors indicated competition between E8, E62A1, and E65E8 and the peripheral-site inhibitors BW284c51 and propidium, but not with the active-site inhibitors eserine and edrophonium. Fluorescence titration between antibodies and propidium confirmed these results. We conclude that the adhesion function of acetylcholinesterase is located at the peripheral anionic site. This has implications, not only for our understanding of neural development and its disorders, but also for the treatment of neuroblastoma, the leukemias, and Alzheimer's disease. Copyright 1999 Academic Press.

AB There is accumulating evidence that **acetylcholinesterase** has secondary noncholinergic functions, related to adhesion, differentiation, and the deposition of **beta-amyloid** in Alzheimer's disease. We have observed that the specific **acetylcholinesterase** peripheral anionic site inhibitors, BW284c51 and propidium iodide, abrogated cell-substrate adhesion in three human neuroblastoma cell lines.
The active-site inhibitors,. . .

TI Beta-amyloid levels predict cholinesterase activity in human cerebrospinal fluid.

AU Carroll R T; Lust M R; Emmerling M R
CS Neuroscience Therapeutics, Parke-Davis Pharmaceutical Research Division, Warner-Lambert Co., Ann Arbor, MI 48106, USA.

SO NEUROREPORT, (1999 Jan 18) 10 (1) 127-30.
Journal code: A6M. ISSN: 0959-4965.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199907
EW 19990705

AB There is increasing evidence suggesting that **beta-amyloid** (Abeta) has a direct influence on cholinergic activity. In particular, Abeta has been shown to induce the expression of **acetylcholinesterase** in the brains of CT-100-expressing transgenic mice and in cell culture experiments. These data indicate a link exists between Abeta production and acetylcholinesterase expression in the human CNS. To test this hypothesis, Abeta levels and cholinesterase activity were measured in 110 human CSF samples. Abeta levels were found to have a significant and positive correlation with cholinesterase activity. This correlation was particularly strong in individuals > 50 years of age. These data support the hypothesis that Abeta can effect cholinergic activity and that this effect may be enhanced in the elderly.

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TI **Acetylcholinesterase** is increased in the brains of transgenic mice expressing the C-terminal fragment (CT100) of the **beta-amyloid** protein precursor of Alzheimer's disease.

AU Sberna G; Saez-Valero J; Li Q X; Czech C; Beyreuther K; Masters C L; McLean C A; Small D H

CS Department of Pathology, University of Melbourne and Mental Health Research Institute of Victoria, Parkville, Australia.

SO JOURNAL OF NEUROCHEMISTRY, (1998 Aug) 71 (2) 723-31.
Journal code: JAV. ISSN: 0022-3042.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199810

EW 19981004

AB Acetylcholinesterase (AChE) expression is markedly affected in Alzheimer's disease (AD). AChE activity is lower in most regions of the AD brain, but it is increased within and around amyloid plaques. We have previously shown that AChE expression in P19 cells is increased by the amyloid beta protein (A beta). The aim of this study was to investigate AChE expression using a transgenic mouse model of A beta overproduction. The beta-actin promoter was used to drive expression of a transgene encoding the 100-amino acid C-terminal fragment of the human amyloid precursor protein (APP CT100). Analysis of extracts from transgenic mice revealed that the human sequences of full-length human APP CT100 and A beta were overexpressed in the brain. Levels of salt-extractable AChE isoforms were increased in the brains of APP CT100 mice. There was also an increase in amphiphilic monomeric form (G1A) of AChE in the APP CT100 mice, whereas other isoforms were not changed. An increase in the proportion of G1A AChE was also detected in samples of frontal cortex from AD patients. Analysis of AChE by lectin binding revealed differences in the glycosylation pattern in APP CT100 mice similar to those observed in frontal cortex samples from AD. The results are consistent with the possibility that changes in AChE isoform levels and glycosylation patterns in the AD brain may be a direct consequence of altered APP metabolism.

TI **Acetylcholinesterase** is increased in the brains of transgenic mice expressing the C-terminal fragment (CT100) of the **beta-amyloid** protein precursor of Alzheimer's disease.